IN THE SPECIFICATION:

Please amend paragraph **[0005]** as follows:

[0005] In the present invention we have identified a novel substrate for presenilin. More specifically, a specific interaction of the type I transmembrane protein telencephalin (TLN) with PS1 and PS2 is found. TLN is a neuron and region specific member of the ICAM subfamily of intercellular adhesion molecules (Hayflick et al., 1998; Yoshihara and Mori, 1994). It has been shown that TLN promotes dendritic outgrowth (Tamada et al., 1998; Tian et al., 2000) and contributes to long-term potentiation (Nakamura et al., 2001; Sakurai et al., 1998). The analogy with Notch in promoting dendritic branching (Berezovska et al., 1999; Sestan et al., 1999), and the downregulation of TLN in the brains of AD-patients (Hino et al., 1997), motivated us to investigate the PS1-TLN interaction in detail. We have delineated precisely the binding sites in PS1 and TLN, and can extend those investigations towards APP. Our findings can be integrated into a novel binding model for presenilins with type I transmembrane proteins. Two domains at opposing sites in the PS1 sequence are involved in TLN and also in APP binding. Our results therefore indicate that type I integral membrane proteins can bind via their transmembrane domain to a common binding pocket constituted by the carboxyterminal domain and the first integral membrane domain of PS1. We could not demonstrate any binding *in vitro* between APP, nor TLN (or fragments derived thereof) with the hydrophilic N-terminus of PS1. The fact that the binding domains we identified in PS1 are exceptionally well conserved among different species further corroborates our hypothesis that they are of major functional importance. Consistently, only few disease-linked mutations are found in these regions (Cruts and Van Broeckhoven, 1998; see also AD Mutation Database, ~~molgen-www.uia.ac.be/ADMutations~~) while some loss-of-function mutations in these domains in the PS homologues of *C. elegans* (Arduengo et al., 1998; Levitan and Greenwald, 1995; Okochi et al., 2000) and *Drosophila* (Lukinova et al., 1999) have been reported. If both domains, as we demonstrate here, comprise together a functional pocket binding the transmembrane regions of TLN and APP, they should be spatially closely juxtaposed to each other. This indicates for a circular or ring-like structure for PS1. Such a model supports recent findings that intramolecular associations between different domains of PS1 as well as cooperative interactions between both fragments are important for the functionality of the PS complex (Saura et al., 1999; Tomita et al., 1998).